Remarks

Claims 1, 2, 4-8, and 10-18 were pending. Claims 1, 2, 4, 8, 10-12, 14, and 17 are canceled; claims 13, 15, 16, and 18 are amended; and new claims 19-24 are added herein. As a result, claims 13, 15-16, and 18-24 are now pending. Claims 13, 15-16, 18-19, and 22 read on the elected species of an in vitro screening method.

The new and amended claims are supported throughout the originally filed specification and claims. Claims 13 and 16 are supported, e.g., by the corresponding originally filed claims. Claims 15 and 18 are supported, e.g., by originally filed claims 15 and 18; at page 20, line 20 to page 21, line 1; and at page 21, lines 12-15. Claims 19 and 21 are supported, e.g., by originally filed claim 14. Claim 20 is supported, e.g., by originally filed claim 14 and at page 1, line 13. Claims 22 and 24, are supported, e.g., by originally filed claim 17. Claim 23 is supported, e.g., by originally filed claim 17 and at page 1, line 13.

Objections to the Specification and IDS

The Examiner objected to the specification as identifying the application as a continuation application rather than a divisional application. The first paragraph of the specification is amended herein to correct this.

The Examiner indicated that many of the references cited in the Information Disclosure Statement and cited in an earlier parent application were lost by the U.S.P.T.O. Applicant submits copies of the references with this Amendment. Applicant also submits a Supplemental IDS and copies of the two references cited therein.

The Examiner objected to the Brief Description of the Drawings for not specifically identifying and describing panels 2A and 2B in Fig. 2 at the paragraph beginning at page 8, line 18. This paragraph is amended herein to address this concern.

Objections to the Claims

The Examiner objected to claims 13-18 as encompassing non-elected inventions. Applicants respectfully traverse this objection.

The requirement to elect in vitro or in vivo screening was an election of species requirement, not a restriction requirement. The Examiner wrote with the election of species requirement:

> Upon allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species MPEP § 809.02(a).

Thus, the Examiner indicated that the generic claims 13 and 16 would be examined and that the applicant is entitled to additional species (additional to the in vitro species elected) that are written in dependent form. Claims 20, 21, 23, and 24 are directed to in vivo testing and are written in dependent form, depending from the generic claims 13 and 16. Claims 13, 15-16, 18-19, and 22 read on the elected species of in vitro testing.

Rule 146 ("Election of Species") states "In the first action on an application containing a generic claim to a generic invention (genus) and claims to more than one patentably distinct species embraced thereby, the examiner may require the applicant in the reply to that action to elect a species of his or her invention to which his or her claim will be restricted <u>if no claim to the genus is found to be allowable.</u>" 37 C.F.R. 1.146, emphasis added.

Claims 13 and 16 are generic linking claims, linking claim 19 with 20 and 21 and claim 22 with 23 and 24. M.P.E.P. § 809 states that restriction is allowed when linking claims are present, but "the linking claims must be examined with the invention elected." It goes on to state: "Should any linking claim be allowed, the restriction requirement must be withdrawn." That shows that the linking claim must be examined over its entire scope.

Thus, the Applicants are not obligated to amend claim 13 and 16 to recite in vitro testing in response to the election of species requirement. Rather, the Examiner is obligated under her own statement in the election of species requirement, under 37 C.F.R. 1.146, and under M.P.E.P. § 809 to examine the generic claims 13 and 16 and to allow

consideration of claims directed to additional species written in dependent form upon allowance of a linking claim.

Accordingly, Applicants respectfully request withdrawal of the objection to claims 13-18.

The Rejection of the Claims Under 35 U.S.C. §112, Second Paragraph

Claims 13-18 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is respectfully traversed.

The Examiner asked of step (a) in claims 13 and 16, "Are the osteoblasts and osteocyte cells together in the same preparation or are they separate?" Claims 13 and 16 recite in step (a) "contacting osteoblast and osteocyte cells with either a glucocorticoid or a test compound." Thus, the claims are clear that osteoblast and osteocyte cells are contacted with either a glucocorticoid or a test compound. Since the claims do not recite either that the osteoblast and osteocyte cells are together in a mixture or are separate, they may be either. That does not make the claim indefinite. Breadth is not indefiniteness. M.P.E.P. § 2173.04.

The Examiner stated that it was unclear in step (b) which cells are referenced by "said cell," osteoblasts or osteocytes or both. Applicants believe there is nothing unclear about the reference to "said cells." "Said cells" refers to the cells recited earlier in the claim, which are osteoblast and osteocyte cells. Nonetheless, to facilitate prosecution the phrase is amended herein to "said osteoblast and osteocyte cells."

The Examiner goes on to quote in step (b) "treatment with said glucocorticoid and said test compound," and asks whether this step entails treating cells with glucocorticoid alone, or a test compound alone, or both compounds at the same time. The contacting cells with either glucocorticoid or a test compound is recited in step (a). The "either . . . or" language of step (a) makes it clear that one group of cells is contacted with the glucocorticoid and another group separately with the test compound. Step (b) in both claims 13 and 16 is amended to recite "comparing the number of said osteoblast and osteocyte cells undergoing apoptosis following treatment with said glucocorticoid to the number of said osteoblast and osteocyte cells undergoing apoptosis following treatment

with said test compound," and this language reinforces that one group of cells is contacted with the glucocorticoid and another group separately with the test compound in order to allow comparing the number of cells undergoing apoptosis in the two conditions.

The Examiner also pointed out that the exact same method steps were recited in claims 13 and 16. Claim 16 is amended to recite in step (b) "wherein a lower number of apoptotic cells following treatment with said test compound than with said glucocorticoid is indicative of a compound that increases bone mineral density." This differentiates claim 16 from claim 13.

The Examiner stated that claims 15 and 18 were vague in whether Applicants intended to select from a group of assay techniques and in whether the techniques included fragmenting DNA or assaying for DNA fragmentation. Claims 15 and 18 have been amended to address this concern, and Applicants believe the amended claims are clear.

In view of the amendments and remarks herein, Applicants respectfully request withdrawal of the rejection of claims 13-18 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Rejection of the Claims Under 35 U.S.C. §102

Claims 13-18 were rejected under 35 U.S.C. 102(b) as being anticipated by Jilka et al. (1997) *J. Bone and Mineral Res.* 12 (supplement): S455, abstract S411. This rejection is respectfully traversed.

Claims 13, 15-16, and 18-24 recite screening methods involving (a) contacting osteoblast and osteocyte cells with either a glucocorticoid or a test compound; and (b) comparing the number of said osteoblast and osteocyte cells undergoing apoptosis following treatment with said glucocorticoid to the number of said osteoblast and osteocyte cells undergoing apoptosis following treatment with said test compound.

Jilka et al. discloses investigating the effect of glucocorticoids and the IL-6 cytokine on apoptosis in primary cultures of bone marrow cells stimulated to differentiate into osteoblasts. Jilka et al. reports contacting bone marrow cells with dexamethasone beginning after 6 days of culture. The abstract discloses that bone marrow cell cultures

contacted with dexamethasone produced more apoptotic cells than untreated control cultures after 10 days of culture and after 20-30 days of culture. Jilka et al. discloses that if IL-6 was added to the cultures 24 hours before dexamethasone was added, it decreased dexamethasone-induced apoptosis. Jilka et al. discloses that in the 20-30 day cultures, some of the apoptotic cells had characteristics suggesting they were osteoblasts.

A reference anticipates a claim under 35 U.S.C. § 102, "only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. §2131; *Verdegaal Bros. v. Union Oil Co. of California* 814 F.2d 628,631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). The pending claims recite contacting osteoblast and osteocyte cells with either a glucocorticoid or a test compound. Applicants discovered that the increase in apoptosis with glucocorticoid treatment was more dramatic in osteocytes than osteoblasts. The percentage of osteoblasts undergoing apoptosis increased 3-fold in mice treated with prednisolone (page 28, lines 17-19), whereas the percentage of osteocytes undergoing apoptosis increased by an infinite factor, going from none in the controls to 28% in the prednisolone-treated mice (page 29, lines 8-10). In contrast, Jilka et al. discloses only contacting bone marrow containing osteoblast progenitor cells with a glucocorticoid. Osteocytes are not disclosed to be present. Therefore, Jilka et al. does not anticipate any of the present claims.

In addition, Jilka et al. discloses contacting the bone marrow osteoblast progenitor cells with a glucocorticoid (dexamethasone), or with the glucorticoid plus IL-6. In contrast, the pending claims recite contacting the osteoblast and osteocyte cells with either a glucorticoid or a test compound.

Furthermore, the pending claims recite methods of screening for compounds that stimulate bone development or increase bone mineral density. The claims recite comparing the number of osteoblast and osteocyte cells undergoing apoptosis following treatment with a glucocorticoid to the number undergoing apoptosis following treatment with a test compound, wherein a lower number of apoptotic cells following treatment with said test compound than with said glucocorticoid is indicative of a compound that stimulates bone development (claims 13, 15, and 19-21) or indicative of a compound that increases bone mineral density (claims 16, 18, and 22-24). Jilka et al. does not disclose

or suggest any screening program. It does not disclose that a lower number of apoptotic cells following treatment with a test compound than following treatment with a glucocorticoid is indicative of a compound that stimulates bone development or that it is indicative of a compound that increases bone mineral density.

Since Jilka et al. does not disclose all of the elements of any of the pending claims, it does not anticipate any of the present claims. Therefore, Applicants respectfully request withdrawal of the rejection of claims 13-18 under 35 U.S.C. § 102(b) over Jilka et al.

Conclusion

Applicants believe that the claims are in condition for allowance. The Examiner is invited to telephone Applicant's attorney (651-207-8270) to facilitate prosecution of this application.

Respectfully submitted,

STAVROS C. MANOLAGAS ET AL.

By their Representatives,

McTavish Patent Firm
429 Birchwood Courts
Birchwood, MN 55110
651-207-8270

Date Apr. 27, 2006 By: Hugh McTavish

Hugh McTavish
Reg. No. 48,341

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient first class postage, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this day of April 27, 2006.

Hugh McTavish